REMARKS

Claims 1 and 3-13 are pending. Claims 1, 4, 7, 10, and 12 have been amended.

The amendments to claims 4, 7, and 10 merely correct typographical errors in the names of several active agents. The Applicants believe that these changes do not constitute the addition of new matter, as each agent was identified by its primary purpose, and the spelling errors were clearly typographical in nature. One of ordinary skill in the art would have easily been able to infer the correct spellings of the intended agents.

Importantly, the claim amendments should not be construed to be an acquiescence to any of the claim rejections. Rather, the amendments are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to prosecute further the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

RESPONSE TO CLAIM REJECTIONS UNDER 35 USC § 112

Claims 1 and 3-13 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that there is no support for the amendments, of April 13, 2009, that added the limitation of "the oil phase of the emulsion is about 0.5% to about 3.0% by weight of the emulsion."

Solely to expedite prosecution, claims 1 and 12 have been amended to limit the oil phase of the emulsion to "0.8% to 6.0%" by weight of the emulsion. Support for this amendment can be found in Examples 1-3, as noted by the Examiner.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶ 1.

RESPONSE TO CLAIM REJECTIONS UNDER 35 USC § 103(a)

To establish a *prima facie* case of obviousness, a number of criteria must be met. For example, all of the limitations of a rejected claim must be taught or suggested in the references relied upon by the Examiner; or they must be among the variations that would have been "obvious to try" to one of ordinary skill in the relevant art in light of the cited references.

Moreover, one of ordinary skill in the relevant art must have a reasonable expectation of success in light of the combination of cited references. Importantly, the reasonable expectation of success must be found in the prior art, and may not be based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); see MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

Tamarkin 1 in view of Davis and Sachetto

The Examiner contends that claims 1 and 3-13 are unpatentable over Tamarkin 1 (US 2006/0140984) in view of Davis (US 5,143,717), in further view of Sachetto (WO 96/03115). The Applicants respectfully traverse.

As noted by the Examiner, the combined teaching of Tamarkin 1 and Davis does not include all of the limitations of the rejected claims because, for example, neither document discloses a hydrofluoroalkane propellant. The Examiner asserts that this deficiency is cured by Sachetto.

Assuming *arguendo* that all of the limitations of a rejected claim are taught or suggested in the references relied upon by the Examiner, or that any missing limitations are among the variations that would have been "obvious to try," the Applicants respectfully assert that there was no reasonable expectation of success in using hydrofluorocarbon propellants for immediate foaming compositions.

Sachetto describes aqueous foamable compositions comprising active agents, surfactants and foaming agents. The foaming agents described are liquefied gases, such as propane, butane, isobutene, as well as HFA 134a and HFA 227 (page 4, and table 1). However, the only exemplification provided is for compositions comprising butane as the foaming agent; no compositions comprising HFAs are exemplified, and Sachetto provides no teaching as to why butane and HFAs would reasonably be considered interchangeable.

Moreover, in contrast to the claimed invention, the compositions described by Sachetto feature *delayed* foaming action. Sachetto takes pains to differentiate the disclosed delayed foaming compositions from immediate foaming compositions otherwise known in the art. In this regard, Sachetto teaches away from the using a hydrofluorocarbon propellant for an immediate foaming composition. Pertinently, it is improper to combine references where the references

teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. One of ordinary skill in the art would have appreciated that the formulations for delayed foaming compositions and immediate foaming compositions are not the same. Therefore, given the guidance provided by Sachetto, one of ordinary skill in the art would not have considered it reasonable to use in an immediate foaming composition a propellant used solely in a delayed foaming composition.

Moreover, to support the Applicants' assertion that one of ordinary skill in the art would not have had a reasonable expectation of success based on the art cited by the Examiner, the Applicants provide **Exhibit D** (Smyth, *Advanced Drug Delivery Reviews*, **2003**), and **Exhibit E** (Vervaet, *International Journal of Pharmaceutics,* **1999**). These articles summarize the difficulties associated with replacing CFC propellants with HFA propellants in aerosol formulations. As explained in Exhibit D, in the paragraph spanning pages 812 and 813:

> Initial screening of alternative propellants identified HFA propellants as likely candidates for replacing CFCs. They appeared to have the necessary physical properties: do not deplete ozone, non-flammable, sufficient vapor pressures, and, importantly, they appeared to be as non-toxic and the CFC counterparts. Although toxicological studies relative to the CFC equivalents that were formulated demonstrated the equivalency of HFAs to CFCs, it was quickly realized that ***HFA propellants were not 'drop in' replacements for CFCs*** in pMDIs. (internal citations omitted, emphasis added)

Remarkably, HFA and CFC propellants differ significantly in their polarities and solubilities in water. In addition, they differ significantly in their ability to dissolve pharmaceutical active ingredients and common pharmaceutical surfactants. Exhibits D and E further explain the then-widespread belief that it was necessary, for example, to incorporate volatile lower alcohols as co-surfactants in order for HFA propellants to function as replacements for CFC propellants. For example, the abstract of Exhibit E explains that:

> [c]onventional (CFC soluble) surfactants are effectively insoluble in the major CFC replacement candidates, HFA 134 and HFA 227ea, in the absence of co-solvents. While these ethane and propane derivatives have comparable boiling points and vapor pressures to dichlorodifluoromethane

> (CFC 12), their increased polarity demands that formulators use either alternative (soluble) surfactants, or co-solvents along with traditional surfactants, in order to stabilize pressurized suspension products.

In other words, one of ordinary skill in the art would have understood that one cannot simply take a composition which contains a CFC and substitute an HFA with any reasonable expectation of success in maintaining the efficacy of the original formulation. Moreover, because the rejected claims specifically require that the formulations "not contain volatile lower alcohols" nor contain "co-solvents or co-propellants" (i.e., the very things which are suggested in the art to make HFA formulations workable), the Applicants respectfully assert that based on the state of the art, as summarized by Exhibits D and E, one of ordinary skill in the art would not have had a reasonable expectation of success in preparing the claimed formulations.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

Tamarkin 2 in view of Quigley, Jr. and Sachetto

The Examiner contends that claims 1 and 3-13 are unpatentable over Tamarkin 2 (US 2006/0233721) in view of Quigley, Jr. (US 6,075,056), in further view of Sachetto (WO 96/03115). The Applicants respectfully traverse.

As noted by the Examiner, the combined teaching of Tamarkin 2 and Quigley, Jr. does not include all of the limitations of the rejected claims because, for example, neither document discloses a hydrofluoroalkane propellant. The Examiner asserts that this deficiency is cured by Sachetto.

Again, assuming *arguendo* that all of the limitations of a rejected claim are taught or suggested in the references relied upon by the Examiner, or that any missing limitations are among the variations that would have been "obvious to try," the Applicants respectfully assert that there was no reasonable expectation of success in using hydrofluorocarbon propellants for immediate foaming compositions.

Sachetto describes aqueous foamable compositions comprising active agents, surfactants and foaming agents. The foaming agents described are liquefied gases, such as propane, butane, isobutene, as well as HFA 134a and HFA 227 (page 4, and table 1). However, the only exemplification provided is for compositions comprising butane as the foaming agent; no

compositions comprising HFAs are exemplified, and Sachetto provides no teaching as to why butane and HFAs would reasonably be considered interchangeable.

Moreover, in contrast to the claimed invention, the compositions described by Sachetto feature *delayed* foaming action. Sachetto takes pains to differentiate the disclosed delayed foaming compositions from immediate foaming compositions otherwise known in the art. In this regard, Sachetto teaches away from the using a hydrofluorocarbon propellant for an immediate foaming composition. Pertinently, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. One of ordinary skill in the art would have appreciated that the formulations for delayed foaming compositions and immediate foaming compositions are not the same. Therefore, given the guidance provided by Sachetto, one of ordinary skill in the art would not have considered it reasonable to use in an immediate foaming composition a propellant used solely in a delayed foaming composition.

Moreover, the Applicants again point to **Exhibit D** and **Exhibit E** in support of their assertion that one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed invention based on the art cited by the Examiner. The Exhibits summarize the difficulties associated with replacing CFC propellants with HFA propellants in aerosol formulations. As explained in Exhibit D, in the paragraph spanning pages 812 and 813:

> Initial screening of alternative propellants identified HFA propellants as likely candidates for replacing CFCs. They appeared to have the necessary physical properties: do not deplete ozone, non-flammable, sufficient vapor pressures, and, importantly, they appeared to be as non-toxic and the CFC counterparts. Although toxicological studies relative to the CFC equivalents that were formulated demonstrated the equivalency of HFAs to CFCs, it was quickly realized that ***HFA propellants were not 'drop in' replacements for CFCs*** in pMDIs. (internal citations omitted, emphasis added)

Remarkably, HFA and CFC propellants differ significantly in their polarities and solubilities in water. In addition, they differ significantly in their ability to dissolve

pharmaceutical active ingredients and common pharmaceutical surfactants. Exhibits D and E further explain the then-widespread belief that it was necessary, for example, to incorporate volatile lower alcohols as co-surfactants in order for HFA propellants to function as replacements for CFC propellants. For example, the abstract of Exhibit E explains that:

> [c]onventional (CFC soluble) surfactants are effectively insoluble in the major CFC replacement candidates, HFA 134 and HFA 227ea, in the absence of co-solvents. While these ethane and propane derivatives have comparable boiling points and vapor pressures to dichlorodifluoromethane (CFC 12), their increased polarity demands that formulators use either alternative (soluble) surfactants, or co-solvents along with traditional surfactants, in order to stabilize pressurized suspension products.

In other words, one of ordinary skill in the art would have understood that one cannot simply take a composition which contains a CFC and substitute an HFA with any reasonable expectation of success in maintaining the efficacy of the original formulation. Moreover, because the rejected claims specifically require that the formulations "not contain volatile lower alcohols" nor contain "co-solvents or co-propellants" (i.e., the very things which are suggested in the art to make HFA formulations workable), the Applicants respectfully assert that based on the state of the art, as summarized by Exhibits D and E, one of ordinary skill in the art would not have had a reasonable expectation of success in preparing the claimed formulations.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

FEES

The Applicants believe that all of the fees required in connection with the filing of this paper have been provided. Nevertheless, the Director is hereby authorized to charge any additional required fee(s) to our Deposit Account, **06-1448**, reference **CPX-015.01**.

CONCLUSION

In view of the above remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation would expedite prosecution of the application, the Examiner is urged to contact the undersigned.

Respectfully submitted,

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Date: December 22, 2009

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